Chapter 11
Transcription of the Genetic Code: Biosynthesis of RNA

SUMMARY

Section 11.1

- Transcription is the process of using a DNA template to produce RNA
- There are many types of RNA produced, such as messenger RNA, transfer RNA, ribosomal RNA, micro RNA, small interfering RNA, and small nuclear RNA.
- A primer is not needed for RNA synthesis
- As does all polynucleotide synthesis, the reaction proceeds in the 5' to 3' direction.

Section 11.2

- Prokaryotic transcription is catalyzed by RNA polymerase, which is a 470,000 Dalton enzyme with 5 types of subunit, α, ω, β, β', and σ.
- RNA polymerase moves along the template strand of DNA and produces a complementary RNA sequence that matches the coding strand of DNA.
- RNA Polymerase recognizes specific DNA sequences called promoters and binds to the DNA. The promoters tell the polymerase which DNA should be transcribed.
- The σ subunit is loosely bound to RNA polymerase and is involved in promoter recognition.
- Transcription can be divided into three parts – initiation, elongation, and termination.

Section 11.3

- There are four principal control mechanisms for prokaryotic transcription – alternative σ factors, enhancers, operons, and transcription attenuation.
- Alternative σ factors can direct RNA polymerase to different promoters, altering the choice of RNA product.
- Enhancers and silencers are DNA sequences usually found upstream of promoters that stimulate or reduce transcription, respectively. These sequences bind to specific proteins called transcription factors.
- Operons are groups of genes involved in a common metabolic process that are controlled as a group. A common example is the *lac* operon that produces β-galactosidase and other enzymes involved in metabolism of lactose.
- With an operon, a regulatory gene produces either an inducer or a repressor of the operon. A metabolite acts as a co-inducer or co-repressor to affect the transcription of the structural genes.
- Transcription attenuation controls transcription after it has begun by adjusting the level of transcription based on the quantity of a related metabolite. For example, in the trp operon, the level of tryptophan affects the transcription of the genes that produce the enzymes that make tryptophan.

Section 11.4

- Eukaryotic transcription is far more complicated than the prokaryotic version.
- There are 3 principal RNA polymerases in eukaryotes, of which Pol II produces mRNA.
- Pol II is a large protein with at least 12 subunits. Some of the subunits share homology with the subunits of prokaryotic RNA Polymerase as well as with eukaryotic Pol I and Pol III.
- The organization of promoters and enhancers is more complicated with eukaryotes. An important promoter element is the TATA box at -25.
- Initiation of eukaryotic transcription is also much more complicated. In addition to the polymerase and the promoter, there are 6 general transcription factors involved in forming the initiation complex.
- Two other RNA polymerases, pol IV and V, are poorly understood but are involved in producing small non-coding RNA's.

Section 11.5

- Control of eukaryotic transcription includes many of the same concepts seen with prokaryotic transcription.
- The use of enhancers and silencers is more extensive and the promoters are more complicated.
- A protein called Mediator is involved in activation of transcription. Mediator bridges the promoter region and specific enhancers or silencers.
- Activation of eukaryotic transcription is also based on the repression of transcription caused by chromatin structure. The chromatin must be relaxed in order for polymerase to access the DNA.
- Chromatin remodeling complexes and histone modifying enzymes are involved in the relaxation of the chromatin.
- Histones and DNA are modified by methylation, phosphorylation, ubiquitinylation, and acetylation.
- Many control mechanisms are based on response elements, enhancers that respond to some metabolic signal, like heat, heavy metals, or other specific molecules such as cAMP.
- One very important response element is the cyclic AMP response element (CRE). A specific transcription factor called CREB and a mediating protein called CBP are involved in many metabolic processes in eukaryotes.
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Section 11.6

- Most of the transcription of DNA to RNA does not lead to RNA's that code for proteins, rather it leads to non-coding RNA
- The two principal types of non-coding RNA's are micro RNA's (MiRNA) and small interfering RNA's (SiRNA)
- Micro RNAs are about 22 nucleotides long, and are cut from a longer, hairpin-shaped RNA by the enzyme Dicer. MiRNAs bind imperfectly to specific mRNAs and block their transcription.

- SiRNAs are formed in a way similar to miRNA, by the enzyme Dicer. When a cell detects specific double-stranded RNA molecules, Dicer cuts them into small pieces of 21–25 nucleotides. These then bind to mRNA molecules in the process known as RNA interference (RNAi), targeting them for destruction.

Section 11.7

- Proteins such as transcription factors that bind to DNA often have recognizable structural motifs.
- Common motifs are the helix-turn-helix, zinc fingers, and basic-region leucine zippers.
- The fact that many transcription factors and other DNA binding proteins have such motifs has aided in the identification of these proteins when they are initially discovered.
- In addition to binding DNA, many proteins involved in transcription bind to other proteins.
- Many protein-protein binding domains also have identifiable motifs, such as acidic domains, glutamine-rich domains, and proline-rich domains.

Section 11.8

- After being transcribed from DNA, many RNA molecules are modified, often extensively, before they arrive at their final form.
- Several modifications are common with tRNA and rRNA, such as trimming, addition of terminal sequences, and base modification.
- Messenger RNA is modified by putting a cap on the 5’ end and a poly-A tail on the 3’ end.
- Messenger RNA is also modified by the removal of intervening sequences, or introns.
- The reaction that removes introns involves the formation of a lariat as an intermediate. Splicing also depends on a separate type of RNA called a small nuclear ribonucleoprotein, or snRNP (pronounced snurp).
- Alternative splicing of mRNA helps account for the fact that there are more proteins produced in eukaryotes than there are separate genes.

Section 11.9

- Proteins are not the only biological molecules with catalytic properties. Some RNAs, called ribozymes, also catalyze certain reactions.
- Group I ribozymes require an external guanosine for reactivity. Group II ribozymes do not have this requirement. They carry out catalysis via a lariat mechanism.

LECTURE NOTES

Most students will have seen much of the material in this chapter in earlier courses, particularly in beginning biology courses, but they are unlikely to have gone into any of the molecular details. A good method of presenting this information is to point out similarities and differences between DNA replication (chapter 10) and the

material covered here. In this manner each topic reinforces the other. This chapter is likely to comprise two full lectures.

LECTURE OUTLINE

I. Transcription in prokaryotes
   A. RNA polymerase in *E. coli*
      1. Core vs. holoenzyme
      2. Template vs. nontemplate strand
      3. The promoter locus and □-subunit
   B. Promoter structure
      1. Transcription start site
      2. Pribnow box
      3. –35 region
      4. Core promoter and UP sequences
   C. Chain initiation
      1. Closed complex formation
      2. Open complex formation
   D. Chain elongation
   E. Chain termination
      1. Intrinsic termination
      2. ρ-dependent termination

II. Regulation of transcription in prokaryotes
   A. Alternative σ factors
   B. Enhancers
      1. Enhancers
      2. Transcription factors
      3. Silencers
   C. Operons
      1. Induction
      2. Regulatory vs. structural genes
      3. Operators
      4. Catabolite repression
      5. Positive and negative regulation
      6. Co-repressors and autoregulation
   D. Transcription attenuation in the trp operon

III. Eukaryotic transcription
   A. RNA polymerase variants
   B. RNA pol II structure
   C. Pol II promoters
      1. Upstream elements – enhancers and silencers
      2. TATA box
      3. Initiator element and transcription start site
   D. Transcription initiation
      1. General transcription factors
      2. Preinitiation complex formation
   E. Elongation and termination

IV. Regulation of transcription in eukaryotes
- A. Basal level transcription
- B. Enhancers and silencers
- C. Response elements
  1. General categories
  2. cAMP-response element as an example

V. Non-Coding RNA's
- A. Micro RNA's
- B. Small Interfering RNA's
- C. RNA Silencing

VI. Structural motifs in DNA-binding proteins
- A. DNA-binding domains
  1. Helix-Turn-Helix motifs
  2. Zinc fingers
  3. Leucine zipper motifs
- B. Transcription-activation domains
  1. Acidic domains
  2. Glutamine-rich domains
  3. Proline-rich domains

VII. Posttranscriptional modification of RNA
- A. RNA and rRNA
  1. Trimming and catalytic RNA
  2. Addition of terminal sequences
  3. Base modification
- B. mRNA
  1. Capping
  2. Polyadenylation
  3. Splicing out of introns
- C. Details of mRNA splicing
  1. RNPs
  2. Splice sites
  3. Lariat structures
  4. Spliceosomes
- D. Alternative splicing

VIII. Ribozymes
- A. Group I ribozymes
- B. Group II ribozymes

ANSWERS TO PROBLEMS

11.2 Transcription in Prokaryotes

1. No primer is required for transcription of DNA into RNA.
2. RNA polymerase from *E. coli* has a molecular weight of about 500,000 and four different kinds of subunits. It uses one strand of the DNA template to direct RNA synthesis. It catalyzes polymerization from the 5′ end to the 3′ end.
3. The subunit composition for the holoenzyme is $\alpha_2\beta\beta'\sigma$.
4. The core enzyme lacks the σ subunit; the holoenzyme has it.

5. The strand that the RNA polymerase uses as a template for its RNA is called the template strand, the noncoding strand, the antisense strand, and the (–) strand. The other strand, whose sequence matches the RNA produced except for the T–U change, is called the nontemplate strand, the coding strand, the sense strand, and the (+) strand.
6. The promoter region is the portion of DNA to which RNA polymerase binds at the start of transcription. This region lies upstream (nearer the 3′ end of the template DNA) of the actual gene for the RNA. The promoter regions of DNA from many organisms have sequences in common (consensus sequences). The consensus sequences frequently lie 10 base pairs and 35 base pairs upstream of the start of transcription.
7. Moving from 5′ to 3′ on the coding strand, the order is the following: Fis site, UP element, –35 region, Pribnow box, TSS.
8. Intrinsic termination of transcription involves the formation of a hairpin loop in the RNA being formed, which stalls the RNA polymerase over a region rich in A–U base pairs. This causes termination of transcription and release of the transcript. Rho-dependent termination often involves a similar hairpin loop, but, in addition, a Rho protein binds to the RNA and moves along it toward the transcription bubble. When the Rho protein reaches the transcription bubble, it causes termination.
9. See Figure 11.1. The top DNA strand is the nontemplate strand because it is not used to create the RNA. It is called the coding strand because it has the same sequence as the RNA produced, except for the change of T for U. It is called the sense strand because its sequence would give the correct amino acid sequence of the protein product. It is called the (+) strand again because it has the correct sequence. The bottom strand is called the template strand because it is the one used to make the RNA. It is also the noncoding strand because its sequence does not match the RNA produced. It is the antisense and the (–) strand for the same reason.

11.3 Transcription Regulation in Prokaryotes

10. An inducer is a substance that leads to transcription of the structural genes in an operon. A repressor is a substance that prevents transcription of the structural genes in an operon.
11. The σ factor is a subunit of prokaryotic RNA polymerase. It directs the polymerase to specific promoters and is one of the ways that gene expression is controlled in prokaryotes.
12. σ^{70} is the normal σ-subunit for RNA polymerase in *E. coli.* It directs RNA polymerase to most of the genes that are transcribed under normal circumstances. σ^{32} is an alternate subunit that is produced when the cells are grown at higher temperatures. It directs the RNA polymerase to other genes that need to be expressed during heat shock conditions.

13. The catabolite activator protein is a transcription factor in *E. coli* that stimulates transcription of the *lac* operon structural genes. It responds to cAMP levels such that the *lac* operon is transcribed only when the cells must use lactose as a fuel source.
14. Transcription attenuation is the process found in prokaryotes in which transcription can continue or be prematurely aborted based on the concurrent translation of the mRNA produced. This is often seen in genes whose protein products lead to amino acid synthesis.
15. An operon consists of an operator gene, a promoter gene, and structural genes. When a repressor is bound to the operator, RNA polymerase cannot bind to the promoter to start transcription of the structural genes. When an inducer is present, it binds to the repressor, rendering it inactive. The inactive repressor can no longer bind to the operator. As a result, RNA polymerase can bind to the promoter, leading to the eventual transcription of the structural genes.
16. See Figure 11.5.
17. With phage SPO1, which infects the bacteria *B. subtilis,* the virus has a set of genes called the early genes that are transcribed by the host's RNA polymerase, using its regular σ-subunit. One of the viral early genes codes for a protein called gp28. This protein is another σ-subunit, which directs the RNA polymerase to preferentially transcribe more of the viral genes during the middle phase. Products of the middle phase transcription are gp33 and gp34, which together make up another σ factor that directs the transcription of the late genes.
18. See Figure 11.14. When the level of tryptophan is low, the *trp*tRNA^{trp} becomes limiting. This stalls the ribosome over the tryptophan codons on the mRNA. By stalling the ribosome there, the antitermination loop can form, transcription is not aborted, and the full mRNA is produced. If the ribosome does not stall there, the termination loop forms, and the leader mRNA dissociates.
19. It is the sensing domain of a riboswitch found at the 5' end.
20. It is mRNA that has two functions – sensing and decision making.
21. Translation can be prevented when a hairpin loop forms that blocks the translation initiation site. Another translation halting processes is when a terminator hairpin is created, similarly to the one that forms during transcription attenuation. Also, in the presence of a certain metabolite, such as the sugar glucosamine-6-phosphate (GlcN6P), the mRNA can self destruct.
22. Researchers are hoping to find molecules that can act like a competitive inhibitor and fool the riboswitch into thinking the natural substrate is present. If the riboswitch controls a vital process, then shutting off the riboswitch would kill the pathogen.

11.4 Transcription in Eukaryotes

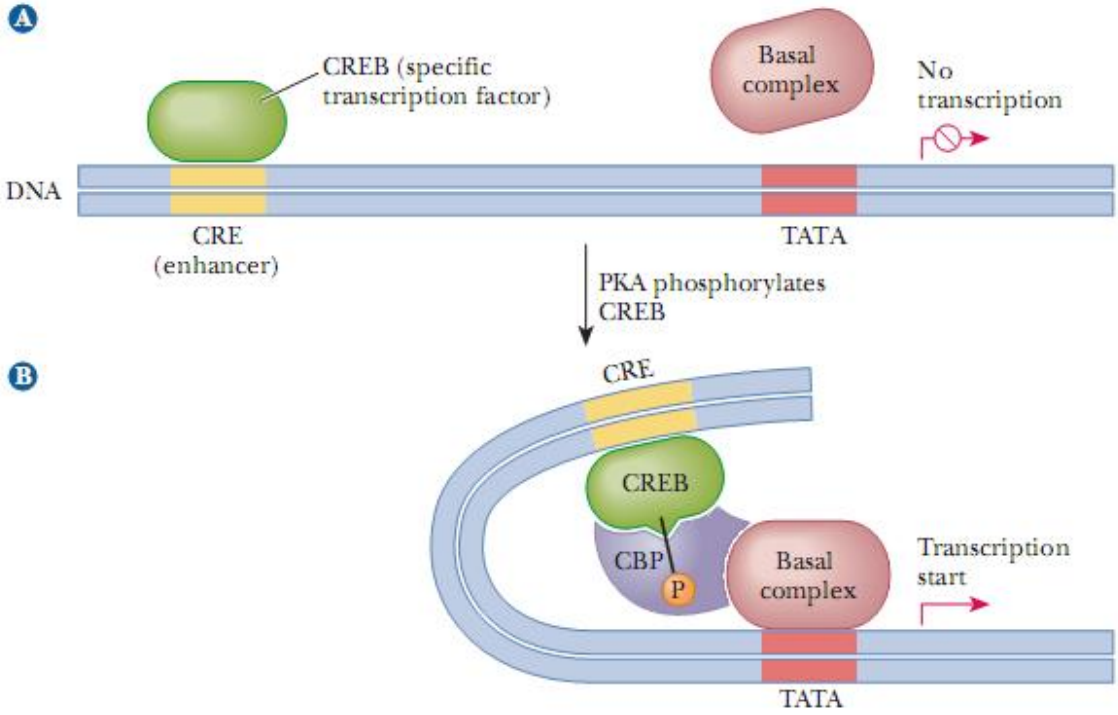
23. Exons are the portions of DNA that are expressed, which means that they are reflected in the base sequence of the final mRNA product. Introns are the intervening sequences that do not appear in the final product, but are removed during the splicing of mRNA.

24. There are three RNA polymerases in eukaryotes, compared with one in prokaryotes. There are many more transcription factors in eukaryotes, including complexes of them necessary for polymerase recruitment. RNA is extensively processed after transcription in eukaryotes, and, in most cases, the mRNA must leave the nucleus to be translated, whereas translation and transcription can occur at the same time in prokaryotes.
25. RNA polymerase I produces most of the rRNA. RNA polymerase II produces mRNA, and RNA polymerase III produces tRNA, the 5S ribosomal subunit, and snRNA.
26. The first component includes a variety of upstream elements, which act as enhancers and silencers. Two common ones are close to the core promoter and are the GC box (–40), which has a consensus sequence of GGGCGG, and the CAAT box (extending to –110), which has a consensus sequence of GGCCAATCT. The second component, found at position –25, is the TATA box, which has a consensus sequence of TATAA(T/A). The third component includes the transcription start site at position +1 and is surrounded by a sequence called the initiator element (*Inr*). The final component is a possible downstream regulator.
27. TFIIA, TFIIB, TFIID, TFIIE, TFIIF, and TFIIH are the general transcription factors. TFIID is also the TATA-box binding protein and is associated with TAFs (TBP associated factors).
28. Its primary function is as a general transcription factor involved in the formation of the open complex for transcription initiation. It binds to the basal unit and is involved in DNA melting through a helicase activity as well as promoter clearance via phosphorylation of the CTD of RNA polymerase. In addition, it also has a cyclin-dependent kinase activity. Thus, TFIIH is involved in tying transcription and cell division together. It is also involved in DNA repair mechanisms.

11.5 Transcription Regulation in Eukaryotes

29. The heat-shock element responds to increased temperature. The metal-response element responds to the presence of heavy metals, such as cadmium, and the cyclic-AMP-response element controls a wide variety of genes based on cAMP levels in the cell.
30. CREB is a transcription factor that binds to the cAMP-response element. It is involved with the transcription of hundreds of genes based on the cAMP levels of the cell. When there is cAMP, CREB is phosphorylated, which allows it to bind the CREB binding protein, which connects the CRE to the basal transcription machinery, stimulating transcription.
31. Regulation in eukaryotes is much more complicated. Prokaryotic regulation is controlled by the choice of σ-subunit, the nature of the promoters, and the use of repressors/inducers. In eukaryotes, there are many more promoter elements, transcription factors, and coactivators. In addition, the DNA must be released from histone proteins, so transcription of DNA is linked to histone modifications.

32. As the mRNA is being produced, ribosomes are bound and begin to translate. A leader sequence on the mRNA leads to a leader peptide. Loops can form in the mRNA in different ways. Some loop combinations lead to transcription termination. The speed with which the ribosome is able to move on the mRNA controls which loop combinations form, and this speed is usually governed by the level of a specific tRNA that is available for the translation.
33. Assuming that there is a basal transcription rate for a particular gene, an enhancer would bind to a transcription factor and lead to a greater level of transcription, while a silencer would bind to a transcription factor and reduce the level of transcription below the basal rate.
34. A response element is an enhancer element that binds to a specific transcription factor and increases the level of transcription of target genes. In the case of response elements, however, this is in response to a more general cell signal, such as the presence of cAMP, glucocorticoids, or heavy metals. Response elements may control a large set of genes, and a given gene may be under the control of more than one response element.
35. As seen here, CREB binds to the CRE. When phosphorylated, it also binds to CBP and bridges to the basal transcription complex.



36. TFIID is one of the general transcription factors for RNA polymerase II. Part of it is a protein that binds to the TATA box in eukaryotic promoters. Associated in complex with the TATA box and the TBP are many proteins called TAFs, for TBP associated factors.
37. The statement is untrue. Many eukaryotic promoters do have TATA boxes, but there are also genes that lack one.

38. Transcription elongation in eukaryotes is controlled in several ways. There are pause sites at which RNA polymerase tends to hesitate. There is also antitermination at which RNA polymerase can transcribe past a normal termination point. The general transcription factor TFIIF stimulates elongation as well as initiation by helping RNA polymerase II read through pause sites. A separate elongation factor, TFIIS, is called an arrest-release factor because it stimulates RNA polymerase to resume transcription once it has hesitated at a pause site. Separate proteins also exist, called P-TEF and N-TEF, that act to positively or negatively affect elongation.
39. CREB is a ubiquitous transcription factor that has been found involved in many genes. It is phosphorylated when cAMP levels are high, which triggers the activation of the genes. CREB-mediated transcription has been implicated in cell proliferation, cell differentiation, spermatogenesis, release of somatostatin, development of mature T cells, protection of nerve cells under hypoxic conditions, circadian rhythms, adaptation to exercise, regulation of gluconeogenesis, transcription regulation of phosphoenolpyruvate carboxykinase and lactate dehydrogenase, and learning and storage in long-term memory.
40. Acidic domains, glutamine-rich domains, and proline-rich domains.
41. Mediator is a giant complex with a mass of over one million Daltons comprising over twenty distinct subunits in yeast, and more than 30 subunits in humans. Mediator bridges the promoter, RNA polymerase and general transcription machinery with specific remote enhancers and silencers.
42. Mediator bridges the promoter region with the enhancer region to activate transcription, or in the opposite case, it binds to the silencer element, but does not recruit RNA pol II to the promoter in this case.
43. Eukaryotic DNA is wound tightly in the nucleosomes. Before the DNA can be transcribed, it has to be available to the transcription machinery, so opening up of the nucleosomes is a necessary first step.
44. The first is the interaction of RNA polymerase with the promoter and transcription machinery. The second is the relief of repression caused by the chromatin structure.
45. Two sets of factors are important: chromatin remodeling complexes that mediate ATP-dependent conformational changes in nucleosome structure and histone-modifying enzymes that introduce covalent modifications into the N-temrinal tails of the histone core octamer.
46. Chromatin remodeling complexes are huge assemblies containing ATP-dependent enzymes that loosen the DNA:protein interactions in nucleosomes by a variety of mechanisms involving sliding, ejecting, inserting, and otherwise restructuring the core octamers.
47. Transcription activation via modification of chromatin involves the covalent modification of histone proteins. In the transcriptionally inactive state, the negative charges on the phosphates of the DNA backbone are tightly bound to the positive charges on the basic proteins of the histone. To activate transcription, this tight binding must be relaxed.
48. There are several families of remodeling complexes. The most well-studied are the SNF/SWI and the RSC families of remodelers.

49. The most important modification of the histones is the acetylation of the ε-amino groups of lysine on the histone tails. Acetylating the lysine removes the positive charge and loosens the binding of the DNA. Other modifications also play a role in transcription regulation through histones, including phosphorylation of serine residues and methylation of lysine and arginine residues.
50. Histones are acetylated by histone acetyltransferases (HATs). They are deacetylated by Histone Deacetylase (HDAC)**.**

11.6 Non-coding RNA's

51. Micro RNAs are about 22 nucleotides long, and are cut from a longer, hairpin-shaped RNA by the enzyme Dicer (These miRNAs bind imperfectly to specific mRNAs and block their transcription.
52. siRNAs are formed in a similar way to miRNA, by the enzyme dicer When a cell detects specific double stranded RNA molecules, Dicer cuts them into small pieces of 21-25 nucleotides. These then bind to mRNA molecules in the process known as RNA interference (RNAi), targeting them for destruction
53. NcRNAs have been linked to many processes, including regular transcription, gene silencing, replication, RNA processing, RNA modification, translation, protein stability, and protein translocation.
54. siRNAs bind to mRNA molecules targeting them for destruction.
55. RNA Silencing is believed to be an evolutionarily conserved process that is analogous to an immune system for protecting our genomes. Researchers have used a variety of techniques to establish the importance of RNA Silencing to the health of the organism, including creating strains of mice that lacked the proteins that made miRNA. The results have highlighted a variety of health problems for the mice, including heart disease and cancer.
56. Loss of miRNA-101 leads to overexpression of a particular histone methyltransferase that helps the progression of prostate cancer.
57. In normal mice, sciatic nerve injury results in loss of nerve function in the muscle and leads to an increase in miRNA-206. Using a line of mice that had ALS and inactivated miRNA-206, the time from onset of the disease was shortened, indicating this miRNA had a protective effect on nerves in the muscle.
58. Work with ALS mice supports a growing body of evidence of the importance of miRNA to neurological function and susceptibility to disease. Micro RNA networks have been implicated in Parkinson's disease, Huntington's disease, and Alzheimer's disease.
59. Dicer and RISC
60. The guide strand is the antisense strand of a double-stranded RNA molecule. The passenger strand is the sense strand.
61. The binding of the siRNA is a perfect match to the mRNA, whereas the binding of miRNA is not perfect, forming a loop.
62. When siRNA binds to the mRNA, the mRNA is degraded by the enzyme Slicer. When miRNA is bound to the mRNA, there is no translation of the message, but the mRNA is not degraded by Slicer.

11.7 Structural Motifs in DNA-Binding Proteins

63. Helix–turn–helix motifs, zinc fingers, and basic-region leucine zippers.

64. The major DNA binding protein motifs are helix–turn–helix, zinc fingers, and basic-region leucine zippers. The helix–turn–helix motifs are organized so that the two helices of the protein fit into the major groove of the DNA. Zinc fingers are formed by combinations of cysteine and/or histidine complexed with zinc ions. A loop of protein forms around this complex, and these loops fit into the major groove of the DNA. Several such loops can be found spiraling around the DNA with the major groove. The basic-region leucine zipper has two domains. One is an area of leucines spaced out every seven amino acids. This puts them on the same side of an α-helix, which allows them to dimerize with another such protein. The basic region is high in lysine and arginine, which bind tightly to the DNA backbone via electrostatic attraction.

11.8 Posttranscriptional RNA Modification

65. Introns are spliced out. Bases are modified. A poly-A tail is put on the 3′ end of mRNA. A 5′-cap is put on mRNA.

66. They both have multiple isoforms created by differential splicing of mRNA.

67. Trimming is necessary to obtain RNA transcripts of the proper size. Frequently, several tRNAs are transcribed in one long RNA molecule and must be trimmed to obtain active tRNAs.

68. Capping, polyadenylation, and splicing of coding sequences take place in the processing of eukaryotic mRNA.

69. The snRNPs are small nuclear ribonucleoprotein particles. They are the site of mRNA splicing.

70. Besides its traditional role in mRNA, tRNA, and rRNA, RNA serves other functions, such as splicing reactions, trimming reactions, and the peptide synthesis reaction of peptidyl transferase. It also has been shown that some small RNAs are produced; they act as gene silencers by binding to specific DNA sequences and blocking their transcription.

71. See Figure 11.37.

72. The Human Genome Project concluded that humans had far fewer genes than previously thought, yet we seem to be more biologically and biochemically complex. One possibility suggested to explain how so few genes could lead to so many proteins is that more proteins may be produced via differential splicing of mRNA. Thus, the same amount of DNA could lead to more gene products.

11.9 Ribozymes

73. A ribozyme is RNA that has catalytic activity without the intervention of protein at the active site. The catalytic portion of RNase P is a ribozyme. The self-splicing rRNA of *Tetrahymena* is the classic example, and it has recently been shown that the peptidyl transferase activity of the ribosome is actually a ribozyme.
74. Two mechanisms for RNA self-splicing are known. In Group I ribozymes, an external guanosine is covalently bonded at the splice site, releasing one end of the intron. The free end of the exon thus produced attacks the end of the other exon to splice the two. The intron cyclizes in the process. (See Figure 11.35.) Group II ribozymes display a lariat mechanism. The 2′-OH of an internal adenosine attacks the splice site. (See Figure 11.39.)
75. Proteins are more efficient catalysts than RNA because they have wider variations in structure and thus can tailor the active site for maximum efficiency for a given reaction.
76. Epigenetics roughly translates to heritable changes in DNA that do not involve a change in the primary structure or sequence of the DNA
77. Epimutations are similar to DNA mutations but affect the DNA scaffolding or modifications without affecting the sequence
78. Over 30 molecules associated with cancer have been found to be chromatin remodelers.
79. Peleg showed that aged mice had a disruption of experience-dependent epigenetic modification of the acetylation site of lysine 12 on histone 4 (H4K12). This was associated with a concomitant loss of normal memory-associated transcription in the hippocampus.
80. They showed that when they infused the mices' hippocampus with an inhibitor of histone deacetylase (HDAC), it increased the acetylation of H4K12, restored memory-associated transcription, and restored behavior memory function.